Respiratory VIVAs (Pharmacology)

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2012.1.3

Question 3 LOA: 1 **SELECTIVE B2 AGONISTS**	What B-receptor types are there? What cellular processes do B-agonist - B-receptor coupling initiate? What are the clinical uses of B2 selective agonists?	B1, B2 + B3 Activation of all 3 receptor types results in stimulation of **adenylyl cyclase** and increased conversion of ATP to cAMP. Mediated by stimulatory coupling protein (Gs) via GDP and GTP **Respiratory**, uterine and vascular smooth muscle relaxation Skeletal muscle K+ uptake	Need B1 + B2 Need adenylyl cyclase Need respiratory bronchodilation + one other

2011.1.2

Drugs used in Asthma	a) What are the effects of corticosteroids on airways in asthma treatment? b) Describe the cellular mechanisms by which corticosteroids are believed to exert their effects acutely.	Increase in airway calibre by **inhibition of airway inflammation, decrease in bronchial reactivity** and local immune suppression 1. Decreased activation of lymphoid cells/eosinophils 2. Decreased cytokine production and action 3. Decreased production vasodilator prostaglandins 4. Decreased histamine release 5. Decreased production of IgE and IgG	bold 2/5 to pass

2009.2.1

Question 2: **Classification of drugs in acute asthma**	(a) Outline the groups of drugs that might be used in asthma and give an example of each?	• **sympathomimetics** • **corticosteroids** • **muscarinic** antagonists • other bronchodilators -magnesium • antihistamines (allergic basis) • methylxanthines • cromolyns • leukotriene inhibitors [antagonists] – montelukast, zafirlukast,zileuton • heliox –changing airflow dynamics • ?other smooth muscle dilators – ketamine; calcium channel blockers • Experimental -; IgE monoclonal antibodies - omalizumab	(2 of 3 bolds to pass) Must get 3 bolded groups and one other with one correct drug example per group to pass.
	(b) Outline the mechanism of action of corticosteroids in asthma	Corticosteroids do the following: • Reduce bronchial reactivity • **Inhibition of** (lymphocytic and eosinophilic) **airway mucosal inflammation** • Increase airway calibre	Must get bolded point to pass

2008.2.2

Question 4: Salbutamol	1). Describe the pharmacokinetics of salbutamol? 2). What are the pros and cons of the different routes of delivery *Prompt: MDI vs nebuliser*	1). Absorption **–complete all routes. Gut** fast, **resp tract slower**- depends on **mechanism delivery - gut 80% with Neb. 2).** Metab/elim- **50% 1st pass** (less if IV) (sulphated- inactive) liver, **rest renal/unchanged. 3). No resp metabolism. 4).** t1/2 3-6hr – prolonged if resp 1.Inhaled- Inhaler/ spacer: targeted/ low dose – minimal systemic ? local effects, co-ordination education; ii) Nebulised- less co-ord required> dose/systemic effects , noisy/frighten children- no benefit in co-ordinated patients 2.Oral- easier in v young/ disabled- longer t1/2, > SE profile, big doses, tachyphylaxis- possible increased deaths 3.IV/IM/SC – useful in asthma extremis or other indications, less 1st pass/. IV- pain/cost/staff use/high SE profile + high risk pts	**good fast absorption- all routes** **Metab 50% + renal.** **Grasp of 2 different routes** Inhaler/ spacer v Neb v IV minimum. Targetted proven effectiveness inhalers/pacers SE profile: < to > Inh v Neb v Oral v Systemic Co-ordination/delivery in extremis (age or severity) important

2008.1.2

Methylxanthine	What are the organ system effects of theophylline ? (Prompt both therapeutic and toxic)	CNS: Mild cortical arousal with increased alertness and deferral of fatigue. Bronchodilation. Nervousness and tremor. Overdose causes medullary stimulation, convulsions and death. CVS: Positive chronotropic and inotropic effects by inhibiting presynaptic adenosine receptors in sympathetic nerves and increasing catecholamine release at nerve endings. Produces tachycardia, increased cardiac output and BP. May cause arrhythmias. GIT: Stimulates gastric acid and digestive enzymes secretion. Kidney: Weak diuretic from increased glomerular filtration and reduced tubular sodium	
	How do these effects of theophylline correlate to its serum concentrations ?	reabsorption. Lung: Bronchodilation by relaxing airway smooth muscle and inhibits antigen-induced release of histamine from lung tissue. Theophylline has a narrow therapeutic window, and its therapeutic and toxic effects are related to its blood level: 5–20 mg/L: Improvement in pulmonary function. Anorexia, nausea, 15-20 mg/L: vomiting, abdominal discomfort, headache, and anxiety occur at concentrations of in some patients: >40 mg/L: Cause seizures or arrhythmias Pass –, CVS & Resp effects, narrow therapeutic window	

Older

Inhaled asthma preventers	Outline the types of drugs used as preventers in the management of asthma?	**Corticosteroids** **Cromolyn** / nedocromil (+/- long acting cromolyn – tilade)	Leukotriene pathway inhibitors (Singular, Accolate): Zafirlukast, montelukast) Long acting antichol; Long acting Beta 2 agonists; Anti IgE monoclonal Ab; Ca channel blockers; Nitric oxide donors
	What are the potential adverse clinical effects of inhaled steroid therapy?	**Oropharyngeal candidiasis** **Any 1 of list**	Hoarseness; Osteoporosis; Cataracts Slows rate of growth in kids; ? delayed puberty
	Describe the mechanism of action of cromoglycate?	**Mast cell stabilisation**	Changed function of delayed Cl channels; inhibits cellular activation: -airway neurones (cough), mast cells, eosinophils
	What are the clinical uses of cromoglycate?	Antigen induced, exercise induced, occupational, young with extrinsic asthma **2 of above** *prompt allowed*	